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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,959	02/28/2005	Lucas Cyril Gerard Van Der Heyden	GRT/4662-2	3062

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EXAMINER	
AUDET, MAURY A	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
08/07/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,959	VAN DER HEYDEN ET AL.	
	Examiner	Art Unit	
	MAURY AUDET	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6-9,11,12,14-21 and 23-26* is/are pending in the application.

4a) Of the above claim(s) *14-18 and 23-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-9,11,12 and 19-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 February 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments within the Appeal Brief filed 3/5/08 have been considered and deemed persuasive. Upon an updated search of the art has been conducted directed to Applicant's position that routinely optimizing molar %'s and molecular weights would not have been prima facie obvious to one of ordinary skill in the art in insulin/diabetic Prosecution has hereby been reopened in order apply a new combination within the art of record deemed to constitute a *prima facie* case of obviousness.

Election/Restrictions

As stated previously, Applicant's election, after the First Office Action on the Merits, with traverse of Group I, composition claims 1-3, 6-9, 11-12, and 19-21 (species peptides with a molecular weight below 500 Da) in the reply filed on 2/9/07 is acknowledged. The traversal is on the ground(s) that it would not be a serious burden to search and examine all groups together. This is not found persuasive because for the reasons of record.

The requirement is still deemed proper and is therefore made FINAL.

Claims 14-18 and 23-26 are withdrawn as begin drawn to non-elected subject matter. Applicant is requested to provide the appropriate claim identifier (, withdrawn) alongside each of these claims, in response hereto. Claims 1-3, 5-9, 11-12, and 19-21 are examined on the merits.

Backdrop

It is again noted, the present application is 371 of PCT/EP03/09790. The related International Search Report and Written Opinion therefrom covers virtually identical claims as

presented here (other than a preliminary amendment to remove multiple dependencies). In Box I.2 of the Search Report it was indicated that "claims 1-18 relate to compositions, uses and methods involving a compound defined by reference to a desirable characteristic or property, namely sensitizing to insulin. [] In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. []A compound cannot be sufficiently defined by its mechanism of action and/or its pharmacologic profile." The International Authorities struggle with the search of the invention based on the claim language/application as filed, is evidenced by the 17 references cited therein, each reading all or in part over the claims. and search thereof.

Notwithstanding the difficulty in searching structure-based subject matter, which is at the core of the present invention, which has been claimed by language to said structures mechanism of action and/or pharmacologic profile; a reasonable and diligent attempt has been made to search/examine the invention as claimed; similar to the problem faced by the International Searching/Examining Authority,. Claims 1-18 are herein examined on the merits.

Information Disclosure Statement

As stated previously, the information disclosure statement filed 4/24/06 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. Only the US references and

International Search Report (part of original filing papers) have been considered, as well as EP 1172373, which the Examiner retrieved on his own and applied below.

Claim Rejections - 35 USC § 102

As stated previously, the rejection of claims 1 and 11-12 under 35 U.S.C. 102(b) as being anticipated WO 01/00223 A2 (Minimed Inc.), has been successfully traversed by the amendment of claim 1 to now require that at least 70 molar% of peptides in the peptide fraction have a molecular weight below 2000 Da. Insulin itself is a 50 amino acid peptide bearing an average weight of 6000 Da. [Applicants arguments however, were not considered persuasive, since the claimed product requires that the composition be suitable for oral consumption, a route which insulin has been administered for some time - a search of the EAST internal database of insulin for oral administration resulted in at least 49 references bearing the same via Title).

Claim Rejections - 35 USC § 103

Below is a new 103 rejection, following an analysis of Applicant's arguments/position within the Appeal Brief. Namely, as to claim 1 requiring that "at least 70 molar% of peptides in the peptide fraction have a molecular weight below 2000 Da". It is noted that the International Authority cited 17 references which were deemed to either read on or render obvious the [asserted amorphously] claimed subject matter of the present invention. The D10 or EP-A-1172373, is still cited merely by example of the same basic thread or them running through all of these references. Namely, that amino acid/peptide fractions obtained by hydrolysis/hydrolysate, capable of being administered via oral route, including with insulin sensitizers, are known in the

art. The Examiner previously stated under 112 2nd (which has been dropped) that "[s]imply put, and until more clearly shown of record, the present invention, especially following amendment (random choice that now "at least 70 molar %" rather than say 30, or 50 of the peptide fraction must be below 2000 Da), appears to be more of a fishing expedition, than a positively recited, particularly pointed out and distinctly claimed invention." The Examiner still finds this somewhat contradictory, as Applicant himself, see former claim 10, previously claimed that composition with a peptide fraction having at least 30 or 50 or 70 molar% below 2000 Da carries out the same, but nonetheless has attempted to more specifically address it would have been predictable for one of ordinary skill in the art to routinely optimize molar/Dalton weights of such fractions. Although the fishing expedition routine optimization within the claimed invention would appear debatable based on the above, the Examiner has moved forward in light of Applicant's assertion that this was not a fishing expedition, conducting an *updated search and analysis focusing on the routine optimization of such parameters as molar %'s and Dalton weights in peptide fractions; e.g. 70 molar% of these amino acid/peptide fractions to be under 2000 Da, which Applicant asserts was not prima facie obvious.*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-3, 6-9, 11-12, and 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP-A-1172373 (Sung Kyu, cited by the International Authority in Applicant's PCT/EP03/09790) in view of Dekker et al. (US 2004/0241664 A1) and Van Loon et al. (US 6,713,082 B2).

EP-A-1172373 is cited merely by example of the volumes of literature on amino acid/peptide fractions, further comprising insulin sensitizers, which may be administered orally (and for diabetic purposes), as cited also by the International Authority. There is not indication that the peptide fraction in EP-A-1172373 does not 70 molar% of a peptide fraction of 2000 Da or less. However, since the reference does not expressly teach that "at least 70 molar% of peptides in the peptide fraction have a molecular weight below 2000 Da" or each and every plausible alternatives, e.g. that the free amino acid be leucine or have a proline on the end.

Dekker et al. teach protein hydrolysate fractions with variable molar %'s (including 61%, nearly the at least 70 molar % Applicant has amended to) and peptides with a molecular weight below 2000 Da (e.g. 400-2000) (see e.g. para's 216 and 247; entire document).

Van Loon et al. teach a composition to enhance blood insulin response comprising a peptide material, free amino acids selected from Leu and Phe, and size limitations of the peptide material (abstract, claims, entire document)

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to administer any routinely optimizable molar %/Dalton weight of a peptide fraction, depending on the desired results, including "at least 70 molar% of peptides in the peptide fraction have a molecular weight below 2000 Da" or modify the amino acid content (e.g. specific peptide fractions/sizes and free amino acids as desired), in the composition of EP-A-1172373, because Dekker et al. advantageously teach peptide hydrolysate fractions containing variable molar %'s (including 61%, nearly the at least 70 molar % Applicant has amended to) and peptides with a molecular weight below 2000 Da (e.g. 400-2000) and Van Loon et al. advantageously teach such peptide fractions/sizes, free amino acids in a composition for enhancing blood insulin response and because EP-A-1172373, like the other volumes of references discussed by the International Authority on Applicant's same claims, similarly teach compositions comprising peptide fragments which enhance blood insulin response (e.g. in diabetic therapy). Absent evidence to the contrary of some unexpected result using "at least 70 molar% of peptides in the peptide fraction have a molecular weight below 2000 Da" or any of the other alternatives claimed, such modifications are merely deemed routine optimizations – similar to if Applicant would have instead amended claim 1 to be "at least 30 molar%".

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MAURY AUDET whose telephone number is (571)272-0960. The examiner can normally be reached on M-Th. 7AM-5:30PM (10 Hrs.).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MA, 8/1/2008

/Maury Audet/
Examiner, Art Unit 1654